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DISCUSSION

GEORGE H. KRESS, M. D. (945 Roosevelt Building, Los Angeles).—Acute iritis will always be a subject of interest, because of the serious damage that can accrue to the eye tissues and functions if proper treatment is not used.

Doctor Rodin has stressed the fact that acute iritis is an emergency disease rather than one in which time can be taken to try this or that alternative therapy. In acute iritis vigorous use of atropin, depending on the stage and intensity of the inflammation, is the first order of the day. Instillation first, with varying dosage as may be indicated, followed by subconjunctival injection, as with epinephren, if hard bound adhesions are present. In severe cases, treatment with the foreign proteins is often given. The value of the salicylates has been well established.

The diagnosis is not always as easy as the classical tables of the textbooks, with vertical columns for iritis, glaucoma and acute conjunctivitis, would indicate. In such cases, cautious but prompt procedures must be instituted to establish the diagnosis along lines indicated by Doctor Rodin. With the above, from the very beginning, a search for the causal factors of the iritic inflammation should be made; and either then or later, according to circumstances, an attempt at elimination of these etiologic factors should be carried out.

❦

SAMUEL A. DURR, M. D. (1006 Medico-Dental Building, San Diego).—Shortly after the speaker's original paper appeared, on the injection of atropin and adrenalin subconjunctivally, I had my only personal experience with this method. The patient was a one-eyed man, aged sixty-five, apparently in good general condition. It was impossible to dilate the pupil by any conservative method, since the patient was seen for the first time, several days after the onset. Fortunately, he was hospitalized. Before the suggested injection was completed, the patient became unconscious, his pulse climbed to 160, his skin was pale and clammy, covered with perspiration as was no doubt my own. The conjunctiva was immediately incised liberally, over the site of the injection, and he was given morphin. I must say that the pupil dilated beautifully, and that he made a perfect recovery. Since then, I have always relied upon instillations of laevo-glaukosan in similar cases, with no untoward results. Horner's report on suprarenin bitartrate, with its rather high percentage of increased intra-ocular tension, caused me to view it with suspicion.

❦

ALFRED R. ROBBINS, M. D. (1930 Wilshire Boulevard, Los Angeles).—Doctor Rodin has clearly pointed out in his paper the type of treatment that a patient with acute iritis has the right to expect from the attending physician:

1. The diagnosis is essential.
2. The treatment must be instituted.
3. The etiological factor must be sought for and corrected.

Treatment is comprised of local and systemic:

A. Local includes—
(*a*) Mydriasis
(*b*) Heat (wet or dry)
(*c*) Counter-irritation (Dionin)
(*d*) Bleeding (leeches)

B. Systemic includes—
(*a*) Specific
(*b*) Nonspecific
(*c*) Removal of foci
(*d*) Bed rest
(*e*) Hyperpyrexia or thermic.

The diagnosis is the basis for any treatment and an uninjured inflamed eye, especially one with little or no discharge, must be considered glaucomatous or iritic until proven otherwise.

Iritic emergency treatment uses atropin, which Doctor Rodin calls the sheet anchor, as the basis of therapy. Mydriasis is essential, and the subconjunctival injection of atropin and epinephrin, as sponsored by Doctor Rodin, is of immense value.

There has been an advance in this treatment since McKenzie's textbook of 1833 advised the rubbing of belladona unguentum into the skin, to the present-day subconjunctival injections of its alkaloid.

The etiology must be established if possible, and a careful physical examination is imperative, as the emergency treatment is only the beginning of the treatment of acute iritis.

Lues, being listed as the cause in 30 per cent to 50 per cent of iritis cases, must be considered first, then Neisserian infection, tuberculosis, and the so-called rheumatic type, with the search for foci done. If diseased sinuses, tonsils, teeth, prostate, etc., are found, they must be treated immediately and surgically corrected if necessary. We all know the startling cures that have been reported after foci removal.

We feel surgical correction should not be delayed, and that the additional disturbance which might result, is rarely harmful, but instead improves the prognosis.

Local treatment may be augmented by leeches for subjective relief at least.

Rest in bed is as important as iris rest, and should be enforced in the acute stage.

Catharsis is desirable, and calomel with saline is still good treatment.

The various alternatives, including salicylates, mercury, iodin, or the arsenicals, can be tried as indicated.

The hyperpyrexia type of treatment, as given by Doctor Rodin, has been developed and extensively used for a variety of inflammatory conditions, including iritis. The endogenous type using foreign proteins is especially valuable. Care must be used, however, in taking the history and in the smalldose tests before using shock-therapy, as deaths have occurred. Gifford's two afebrile days before repeating injections is desirable.

The exogenous hyperthermic therapy, using electrical current or baking cabinets, is newer. This requires special equipment and must be thoroughly tested before being used indiscriminately. It is probably superfluous to add that, in addition to the treatment of the immediate attack, we will be remiss in our duty unless we attempt to ascertain and treat the causative factors, and thus prevent the destructive recurrences of the disease.

RELAPSING FEVER: COMMENTS ON ITS INCIDENCE IN NEVADA

By FRANK C. REYNOLDS, M.D.
Chico

DISCUSSION *by James T. Vance, M. D., Sacramento; Lawrence Parsons, M. D., Reno, Nevada.*

RELAPSING fever was probably first recognized by Hippocrates when he described "bilious remittent malarial fever."[1] However, no further observations were reported until 1744, when Rutty[2] recorded the first epidemic in Ireland. Since this time it has appeared on every continent on the globe except Australia.

IN FOREIGN COUNTRIES

The disease prevailed in Scotland and Ireland during the years 1799-1800, 1817-1819, 1826-1827, and in 1842-1848; the later year included an invasion of the larger cities of England. In 1868-1870, it again appeared in England and Scotland, and cases continued to occur until 1873. Oftentimes it was confused with other forms of fever, and was nearly always associated with circumstances of privation or crowding.

The first accounts coming from Russia were: Odessa in 1833, and from Moscow in 1840-1841. In the autumn of 1863 the disease reappeared in Odessa, spreading to Livonia and Finland in 1865, to Siberia in 1866, and to Poland in 1868. The disease then continued to prevail over extensive areas of Russia until 1878-1879.[1] Since then we have little data, but large infected areas remained, as the alarming number of 1,570,604 cases were reported in 1920.[3]

In Germany a severe epidemic in 1868 resulted from the importation of Russian troops. A second restricted epidemic occurred in 1871-1872, and a third in 1878-1879. Cases have been reported from Italy and Spain, but thus far France and Switzerland have not been affected. Obermeier in 1873 published his observations on the causative spirochete, which he found in the German epidemic of 1868.[4]

The disease has, no doubt, been present in India for many years, but the differential diagnosis between this and the long-continued specific fevers was not clearly made by the early observers. Nothing definite was learned, however, until 1878, when Vandyke Carter described the spirillum which he found in the blood of infected relapsing fever patients.[4] He demonstrated that the clinical course and causative organisms of the relapsing fever there was identical to that found in Europe. The mortality in India is reported to be 5 to 10 per cent. In Africa the disease ranks next to sleeping sickness. However, in America and Europe it is a mild disease. In general, the mortality varies greatly with the different epidemics from nil to as high as 80 per cent.

Up to the time that Livingston, in 1857,[5] reported a peculiar type of relapsing fever from South Africa, often following the bite of a tick, this was only considered to be a disease caused by filth. After this, tick fever was known to spread along the caravan routes from Africa to Asia. Dutton and Todd, in 1904, proved the spirochete of African relapsing fever to be transmitted by a tick. Sargent and Foley, in 1910, proved the European relapsing fever to be transmitted by a louse.

IN NORTH AMERICA

Until the nineteenth century the disease was unknown in North America. In 1844, fifteen cases were reported from Philadelphia, occurring in Irish emigrants. In 1848, a few cases arrived in New York, and in 1850-1851, Dr. Austin Flint saw a number of cases among recent emigrants from Ireland who were received at the Buffalo City Hospital, but no epidemic resulted from these importations. It was not until several years later, 1869-1870, that the disease became epidemic in certain parts of New York and Philadelphia. Parry and Pepper gave the following account relating to its extent and progress: "In Philadelphia, of 1,176 cases in which the date of occurrence is known, there occurred in September (1869), 4 cases; December, 6 cases; January (1870), 5 cases; February, 13 cases; March, 124 cases; April, 209 cases; May, 235 cases; June, 293 cases; July, 115 cases; August, 19 cases; September, 28 cases; October, 15 cases; November, 1 case; December, 2 cases; January (1871), 2 cases; February, 1 case; March, 2 cases; May, 7 cases; June, 2 cases; and October, 2 cases.[1]

IN WESTERN UNITED STATES AND CALIFORNIA

The first recorded epidemic in the western United States was reported by Dr. P. B. M. Miller at Oroville, California.[6] This prevailed during the months of August, September, and October, 1874, and it was estimated that there were several hundred cases among the Chinese laborers. No further mention of the disease was made in California until 1906, when two deaths were recorded in the nineteenth biennial report of the State Board of Health,[7] and in 1907 one death in the twentieth biennial report, although there was no comment as to the location of the laboratory diagnosis.[8]

On the Isthmus of Panama the disease was not recognized prior to 1905. Darling[9] reported that about thirty-one cases were diagnosed in the canal-zone hospitals between 1904 and 1909.

The first cases in native Americans, and confirmed by laboratory diagnosis, were reported in 1915 by Meader.[10] The source of the infection was in Bear Creek Canyon, Colorado. Waring[11] reported another case from this same focus two years later.

In 1921, Briggs gave an account of two patients who became infected at Polaris, California, near Lake Tahoe.[12] Since that time sixty-nine cases have been reported, sixty-six of which have occurred in four foci of the state: Lake Tahoe, Packer Lake, Strawberry Lake, and Big Bear Lake.

Cornick, in 1927, mentioned that relapsing fever was present in Texas,[13] along with a report of eight cases from the Oshman Laboratory in San Angela, Texas. This was followed by a review of four cases by Malcolm Graham in 1931.[14] These occurred in four boys about sixteen years of age who explored a cave in the Colorado River Valley. It is interesting to note that there had been several unreported cases in Llano County previously. In this region, a tick-infested cavern, called the "Blue Bug Cave," was known to cause a strange malady to those who entered it. The people had known this for at least ten years, and over forty cases had occurred from this one focus. On exploration, the sandy floor of the cave was found to be literally covered with ticks. Bannister reported the first cases from Phoenix, Arizona, in 1930.[15] Cases appear sporadically from Utah.

ETIOLOGY

The exciting cause of relapsing fever is a spirochete of the genus Borrelia, which produces a septicemia in man. The different species show no morphologic differences, but on the basis of serologic studies each differs sufficiently to separate them.[16] Borrelia recurrentis in England, Ireland, and other parts of Europe; Borrelia duttoni in Africa; Borrelia novyi in America; Borrelia berbera in Algeria, Tunis, and Tripoli; Borrelia carteri in India; Borrelia persicum in Persia; Borrelia venzuelense in South America; Borrelia

neotropicalis in Panama; and Borrelia histopanicum in Central Africa.

The length varies from 6 to 25 microns, and the width is about 3 microns. There are six to fifteen curves in the body. The organisms are quite actively motile and may be seen by darkfield examination. Division is by transverse fission.[17]

Smears of blood are stained with 20 per cent Giemsa stain for thirty minutes.

MODE OF TRANSMISSION

In Central and Eastern Africa, South America, and in the southwestern part of the United States, the disease is carried from the reservoir hosts by ticks of the genus Ornithodorus-venzuelensis, taljae, turicota, marocanus, thalozani, laharensis, and moubata. In Europe the louse of the genus Pedulus humani, var. corporis and capitis, is responsible for the spread.[18]

After the insect vector has bitten the infected animal, the organisms disappear from the alimentary tract. Six or seven days later, however, the organisms appear in the coelomic cavity, body fluids, and then in all of the body tissues. A tick, once infected, may transmit the disease through three generations; hence the egg, larval, nymphal and adult forms, are all infectious. From clinical histories, it appears that the adult tick is the least dangerous of these, as its presence on the skin of man is usually noticed and may be removed. However, nymphal forms may obtain a blood meal without causing any disturbance to man. This latter fact may account for the lack of knowledge of a previous insect bite. Feces is scratched into the wound from which the blood meal is taken.

The spirochete enters the peripheral blood of monkeys and certain rodents two or three days after their entrance into the tissues. They divide rapidly, and sometimes become more numerous than the red blood corpuscles. Following this stage, which lasts from several hours to several days, they disappear from the blood until another period of rapid multiplication occurs. Usually, after several attacks, antibodies which destroy the spirochetes develop in the host. The same may be said for the disease in man.[19]

Many animals have been found to be able to harbor the infection. The spirochete has been found in the following animals:[20,21] monkey, oppossum, armadillo, calf, horse, cat, chicken, dog, rat, chipmunk, ground squirrel, tamarack squirrel, etc.

The studies of Nicolle and Anderson[22] in Tunis indicate that the spirochete commenced as a parasite of small mammals, and that burrowing rodents serve as the reservoirs of the disease. Similar conclusions were formed by Clark, Dunn, and Benavides in Panama, and Graham reported that the same facts were probably true in Texas.

Spirochetes may pass through the placenta in small numbers without any pathologic changes occurring. Some investigators have found spirochetes in fetal mice. In the new-born, infection takes place during birth. The disease runs a very severe course if infection takes place during pregnancy, and the fetus is found to be immune. Depending on the severity of the epidemic, abortions are more or less frequent.

Muhlens, Grothusen, and others, have found that children and adults may act as carriers of relapsing fever. Spirochetes have been found to remain in the blood stream as long as ninety-eight days after finding the first positive smear. These patients were without symptoms.

AGE AND SEX INCIDENCE

The great predominance of the cases reported have occurred in males. This is undoubtedly due to their greater exposure. No age group has been found to be immune to the infection.

Most infections occur during the summer months of June, July, and August. This period corresponds with the time of appearance and disappearance of the rodents.

PATHOLOGY

Parenchymatous degeneration of the kidneys, heart, and liver has been found with a large, soft spleen which may rupture spontaneously. Not infrequently the organs are bile-stained. The skin is icteric in fatal cases, and there may be petechiae. At times the spleen may show infarction. The bone marrow is hyperemic, with great activity of the leukoblastic elements. The spirochetes have been found in all organs and tissues of the body. None of the changes noted have been characteristic to this particular disease.

SYMPTOMS AND SIGNS

After an incubation period, which varies from six to nine days, the patient becomes acutely ill. Sometimes there is a short prodromal period with malaise and moderate languor. The onset is abrupt, with high fever, chills, intense frontal headaches, and excruciating pains in the back, limbs, and joints. At this time there is usually nausea and vomiting, and there may be some epigastric pain. The fever rises rapidly to 104 or 105 degrees, usually lasting about three days, although these febrile periods may last from two to four days. During the day of onset the fever is high, the second day somewhat lower, and on the third day it begins with a sharp rise and ends by crisis. With this rapid drop of body temperature to normal, there is profuse sweating, and the patient feels quite normal in a few hours except for weakness. Both diarrhea and constipation have been reported.

Without treatment there are usually two to four attacks, but there may be more than ten. While not a strict rule, relapses after the onset are generally less severe.

The afebrile period shows an extreme degree of irregularity. In the moderately severe cases it lasts four to five days. In the severe cases the relapses may appear in two days, or the patient may have a symptom-free period lasting as long as ten days. During this time the patient feels quite well, except for some weakness, and it may be difficult to keep him in bed.

The rash is a very inconstant finding, and when it does occur it seldom lasts more than a day or two. This is of the macular type, appearing on

the trunk and extremities. There seems to be no correlation between the rash and the severity of the symptoms.

During the attack the face is flushed, and the skin is hot and dry with a very toxic appearance. There may be a mild conjunctivitis, and the tongue is usually coated. The mucous membrane of the mouth may show many tiny white papules. The liver may be slightly enlarged and quite tender. Splenic enlargement with tenderness is quite common. The spleen decreases in size between the attacks and becomes larger with each subsequent attack. Jaundice is uncommon. Bronchial findings are not infrequent, but these almost always disappear with the fever. There may be signs of pneumonia in the severely toxic cases. Abdominal distension with urinary retention occurs at times. Irritability and delirium occur at times. The pulse at the onset is 100 to 120, and is full and bounding, while toward the end it grows weaker. This is unlike typhoid in that the pulse is proportionate to the fever.

The white count may be normal or may exceed 15,000, although there is usually a predominance of polymorphonuclear leukocytes. A moderate lymphocytosis may precede the febrile period for two or three days.

The urine may show albumin and casts, but erythrocytes are a rarity.

The Wassermann test is positive in 20 to 50 per cent of these cases, but it becomes negative with the disappearance of the disease.

Sequelae.—Muscular asthenia of variable degree is quite common, and hemorrhagic nephritis, iritis, cranial nerve paralysis, meningitis, pneumonia, polyarthritis, and parotitis have been reported. Abortion has occurred in pregnant women.

TREATMENT

Most cases have been successfully treated by the administration of neoarsphenamin. The dose is the same as that given for antiluetic therapy. This is given during the period of rising temperature rather than during the symptom-free interval when the spirochetes are not predominantly in the blood stream. Usually one dose of sufficient size will affect a cure, but when inadequate amounts of the drug are given, relapses are more prone to occur, and the organisms become more resistant to therapy.

RELAPSING FEVER IN NEVADA

This disease probably has been endemic in the State of Nevada for many years. The first proved case was discovered in Smith Valley in 1930. Since that time there have been thirty known cases, although only ten or twelve have previously been reported. So far, four foci have been found in the State: Lake Tahoe, Gold Park, Smith Valley, and Tonopah.

Of these cases, sixteen have occurred in Smith Valley, six in Gold Park, seven from Lake Tahoe, and one from Tonopah.

This disease is gaining in importance in view of the fact that it is definitely on the increase. Whereas only one case was reported in 1930, eleven appeared in 1935, and four more have been recorded up to August, 1936.

It is evident that a history of tick bites is uncommon, as it appeared in only seven of the thirty cases. However, the region around Gold Park is an exception, as all of the infected patients gave a history of tick bites. In fact, the people in this region have been bitten so often that they paid little attention to tick bites until the occurrence of these cases. After the appearance of this epidemic in 1935, the natives said that there had previously been a similar malady affecting numerous persons fifteen years before, and that several deaths had resulted at that time. However, no other cases appeared during the intervening years, although the people frequently received tick bites from time to time. Thus, we find that the percentage of infected ticks is not great, and is quite contrary to previous findings reported, especially those from the Blue Bear Cave in Colorado, where all those entering the cave were infected.

No cases in which a rash appeared were noted. There was one death in this series: a child, age seven, who succumbed seven days after the first symptom.

The spleen was enlarged in about 50 per cent of the cases, and the liver was enlarged in about 25 per cent. As to constipation or diarrhea there is no constancy. In regard to complications, none appeared.

IN CONCLUSION

Relapsing fever is an ancient disease, being carried by a tick which transmits the spirochete from infected rodents to man. It has probably been endemic in the State of Nevada for many years. To date, four foci have been found. The increasing incidence of the disease is probably due to its better recognition.

Third and Salem streets.

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DISCUSSION

JAMES T. VANCE, M. D. (1127 Eleventh Street, Sacramento).—Doctor Reynold's paper is a most complete statistical report of a comparatively rare disease which may become epidemic under ideal circumstances. It must, therefore, be considered as a real public health problem.

The historical background is very interesting, giving us a panorama of the disease in a few short paragraphs, bringing us up to the present, and dumping the whole affair into our own back yard.

Relapsing fever has created little attention in California, except in the medical schools, because of its rarity. I saw only a prepared slide during four years in San Francisco, and in nine years of practice in Sacramento I was unaware of a single case having been reported from this area. It is quite possible that a diagnosis has occasionally been missed because of inadequate laboratory assistance, or a failure to consider relapsing fever in a differential of the acute fevers. The diagnosis rests with the laboratory, and this is another very good reason why the laboratories, which insist upon doing counting-chamber differential counts, should stop the practice and return to the stained-smear method. Dark-field examination should be done on suspected cases.

Immunologically speaking, it is interesting to note that the disease confers only a passive immunity, lasting from about forty days to six months, leaving the patient just as susceptible as he was before the original attack. This seems to be true of all the spirochetal diseases.

The blood of a relapsing-fever patient remains infectious for a considerable time after the disappearance of symptoms, and even after passage of the blood through a Berkfeld filter. It is, therefore, plain that some manner of public health regulation should be employed in convalescents and intimate contacts, as well as with the active case.

LAWRENCE PARSONS, M. D. (St. Mary's Hospital, Reno, Nevada).—Papers calling attention to relapsing fever in California and Nevada, such as that which Doctor Reynolds, one of my former students, has prepared, are timely and interesting.

We see about half a dozen patients with relapsing fever here in Reno every summer, most of them having acquired their infection at Lake Tahoe during the vacation season. Alert physicians usually suspect the disease by its sudden onset with chills and fever in a previously well individual, and we easily confirm the diagnosis by finding the spirochetes in blood smears with Wright's stain, although sometimes quite a long and even a repeated search are necessary.

One man in Colfax, California, had a severe infection with marked jaundice, and only the blood smears showing numerous spirochetes made the diagnosis of his illness evident.

The tick vector is a very small, pale tick, Ornithodoros hermsi Wheeler, measuring about 5 x 3 millimeters in size. It does not bury itself in the skin like ordinary wood ticks, but drops off after feeding, and most of the patients we have seen had no recollection of having had a tick bite. It is parasitic upon the chipmunk.

An excellent bulletin (No. 61), on Relapsing Fever published by the California State Department of Public Health in 1936. is available to physicians and should be read.

PLASMA CELL MYELOMA AND HYPERPROTEINEMIA*

By I. C. SCHUMACHER, M.D.
O. O. WILLIAMS, M.D.
AND
G. S. COLTRIN, M.D.
San Francisco

DISCUSSION *by Alvin G. Foord, M.D., Pasadena; Harry A. Wyckoff, M.D., San Francisco.*

REIMANN,[1] in 1932, called attention to the fact that autohemagglutination was frequently the result of hyperproteinemia, especially with an increase in the globulin and fibrinogen fractions. In a case diagnosed clinically as arthritis, the abnormal rouleaux formation in smears, and the difficulty encountered on attempting to type the patient's blood, led to plasma-protein studies and the finding of a hyperproteinemia. He suspected myeloma as a causative factor, and this diagnosis was later established. Since Reimann's report, other similar cases of myeloma, showing the interesting phenomenon of autohemagglutination associated with hyperproteinemia, have been recorded in the literature.

Foord[2] reviewed the reported cases of hyperproteinemia in multiple myeloma up to and including the year 1933. In the cases collected, the highest plasma protein encountered was 16 grams per 100 cubic centimeters of blood. Autohemagglutination was noted in only two of them. However, an additional case had an increased sedimentation rate, indicating a possible spontaneous clumping of the red blood cells. To this series he added four cases observed by himself, each of which had a hyperproteinemia with an associated autohemagglutination. The highest plasma protein encountered in Foord's cases was 15 grams per 100 cubic centimeters. Foord and Randall[3] later reported two additional cases showing both autohemagglutination and hyperproteinemia. The total blood proteins in these cases were 18.37 and 12.74 grams per 100 cubic centimeters of blood, respectively. He added at this time three cases from the literature in which the greatest protein encountered was 12.1 grams. Later Sweigert[4] reported a case with total protein estimations ranging from 12.8 to 13.5 grams.

Although increased plasma proteins and the accompanying manifestation of autohemagglutination may be found in conditions other than multiple myeloma, their presence should lead to careful x-ray studies of the bones to rule out this condition. Peters and Eisenman[5] state that increase in globulin is sometimes found in ulcerative tuberculosis, syphilis, and cirrhosis of the liver. However, they found the greatest increase in multiple myeloma and in generalized metastatic carcinoma to the bones. It has been stated that the frequency of hyperproteinemia in multiple myeloma cannot be determined until adequate chemical studies have been made in all cases. On

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